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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/390,634	09/07/1999	PAUL J. PRICE	0942.4190002	7270

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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	29

DATE MAILED: 11/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/390,634	PRICE ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-173* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-173* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *27*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application is a divisional of application 08/781,772, filed January 10, 1997, now abandoned.

On June 24, 2002, an advisory action was mailed (paper number 24) in response to Applicants' amendment filed June 12, 2002, paper number 23, however the previous office action mailed March 12, 2002, paper number 19, was not made final. In a phone conversation with Mr. Cottingham, the error was noted. Examiner indicated that a new office action would be mailed in response to the amendment filed June 12, 2002, paper number 23. After discussion of potential claim amendments addressing the rejections of record, Applicants' requested time for a supplemental response would be filed.

Applicants' amendment filed June 12, 2002, paper number 23, has been received and entered. Additionally, Applicants' supplemental amendment filed November 13, 2002, paper number 26, has been received and entered. Claims 127-154 have been added. Applicants supplemental amendment filed June 11, 2003, paper number 28, has been received and entered. Claims 89-93, 98-103, 105, 106, 108, 109, 117, 118 and 122-134 have been amended. Claims 155-173 have been added. Claims 89-173 are pending and currently under examination.

Response to Amendment

The declaration of Paul J. Price filed under 37 CFR 1.132 filed November 13, 2002, paper number 25, is sufficient in part to overcome a portion of the basis of the rejection of claims 89-126 based upon 35 USC 112, first paragraph. Specifically, the post filing references demonstrating that KOCKOUT™SR can also be used as a serum supplement instead of normal serum to successfully culture primate embryonic stem cells is found persuasive. However, as noted in the basis of the rejection embryonic stem cells for other species have not been isolated nor characterized. The claims are broad encompassing embryonic stem cells from any animal, and dependent claims set forth specific species such as rat, hamster, cow swine, dog, fish, amphibian.... (see claim 95 for example) from which embryonic stem cells have not been obtained. The instant specification does not provide any guidance for the isolation of embryonic stem cells. Given the lack of evidence of the existence of these cells and the difficulty recognized in the art for successfully isolating these cell types from other animals, the declaration fails to provide a nexus to overcome art recognized barriers to obtaining and maintaining these embryonic stem cells from animals not known in the art at the time of filing.

In addition, there is insufficient information to evaluate whether KOCKOUT™SR is a serum supplement specifically supported by the teachings of the present specification. The evidence in the declaration is not sufficient to determine whether given the teachings in the instant specification if one of skill in the art would arrive at the particular formulation of KOCKOUT™SR. It is noted that the particular components of KOCKOUT™SR are not known

or described, therefore while it apparent that a serum replacement can be made and successfully used to culture embryonic stem cells it is unclear if the present specification clearly teaches how to successfully make the serum replacement. Thus, while the evidence of record supports that conditions used to culture mouse embryonic stem cells can successfully used to culture primate embryonic stem cells, the nexus between KOCKOUT™SR and those particular conditions, in particular the specific combination and concentration of serum replacement components taught in the specification are not adequately detailed in the declaration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 89-126 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for culturing murine embryonic stem cells, does not reasonably provide enablement for culturing embryonic stem cells from other species is withdrawn.

It is noted that claims 89-93, 98-103, 105, 106, 108, 109, 117, 118 and 122-134 have been amended to recite and encompass the presence of a medium comprising serum-free medium and a serum-free medium supplement in the methods and products specifically claimed.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as

routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

As reviewed in the instant specification, the art teaches that components in serum are required to maintain embryonic stem cells in culture. Moreover, it is recognized the serum preparations vary from lot to lot, and that testing and characterization of preparations is required to find sources that are suitable for successfully propagating and maintaining embryonic stem cells in culture. To this end, while only mouse and human embryonic stem cells have been isolated and characterized, the methods presently used in other animals are modeled on these successful examples. Though it is maintained that embryonic stem cells from other animals may have characteristics different from that of either mouse or human, as exemplified by the difference in the requirement of LIF between mouse and human, there is no specific evidence

that one could not identify and/or adapt defined culture conditions if these cells types are ever identified. Further, while the inability to successfully isolate these cells from other animals speaks to the lack necessary knowledge in the art for culturing these cells, what appears consistent is that (if) the cells exist in the embryo of other animals, methods will be applied and adapted from those used first to isolate and culture mouse embryonic stem cells and subsequently for human embryonic stem cells. Additionally, based on the yet unsuccessfully efforts in the art to isolate embryonic stem cells from other animals it appears that the skilled artisan expects that modified methods will continue to be explored. Moreover, the art recognizes that even with known methods and materials that testing and optimization is still required and performed routinely. Given these facts as supported by the efforts of the skilled artisans in the art, Examiner would agree that having the methods and materials known and used for culturing mouse and human embryonic stem cells as a starting reference point, that methods for culturing other stem cells will be obtained, in particular providing a precisely defined media absent of the variables of serum recognized as the greatest variable in successfully culturing embryonic stem cells.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 160 and 168 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, the use of the trademark term 'Albumax^{R}'

is improper. If the trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of the 35 U.S.C. 112, second paragraph. *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. In fact, the value of a trademark would be lost to the extent that it became descriptive of a product, rather than used as an identification of a source or origin of a product. Thus, the use of a trademark or trade name in a claim to identify or describe a material or product would not only renders a claim indefinite, but would also constitute an improper use of the trademark or trade name. See MPEP 2173.05(u).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 89-103, 105-111, 117-127, 129, 131, 133, 135, 137,139, 141, 143, 145, 147, 151, 153, 157-159, 161-164, 166, 167, 169-172 are rejected under 35 U.S.C. 102(b) as being anticipated by Ponting (US Patent 5,405,772).

The broad independent claims encompass a product comprising a basal cell culture medium and a serum-free eukaryotic culture medium supplement, use thereof in methods to culture embryonic stem cells, and compositions comprising the embryonic stem cell and the basal cell culture medium with a serum-free eukaryotic culture medium supplement either separate of in a single container. Dependent claims set forth specific species of animals from which the embryonic stem cells are obtained and specific components contained in the serum supplement. Finally claims 124-126 are drawn to a method of producing a recombinant protein using the materials and methods summarized above. Ponting teaches a medium for long term proliferation and development of cells. Beyond basal media commercially available, Ponting provides guidance for obtaining serum free media (starting at column 14, line 57). Ponting teach specific components and preferred ranges thereof to include in the media (see for example Table in columns 12 and 13). Ponting teaches that the media can contain albumin (e.g. human or bovine), transferrin (e.g. human or bovine), growth factors, vitamins, antioxidants, insulin and various trace elements (see columns 9-10, tables and reduction to practice in working examples). Ponting teaches that the media disclosed can be used to culture a variety of cell types including embryonic stem cells (column 8, lines 13-15) including specific reference to known mouse embryonic stem cell lines. Further, Ponting teaches that general culturing methods known in the art can be used to culture a particular cell type, such as providing a feeder cell layer (column 8, lines 30-37). Finally, Ponting teaches that the cells can be used in a variety of methods including

in the production of proteins in culture (column 16, lines 21-31 and 45-64) and methods of differentiation (see column 8, lines 32-42, lines 61-69 and working examples).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 89-173 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ponting.

The claims are summarized above. The remaining claims are drawn to the addition of specific forms of albumin and transferrin, for example iron-saturated transferrin or lipid poor and recombinant albumin, as well as specific growth factors necessary for maintaining mouse

embryonic stem cells in an undifferentiated state, such as the use of LIF. Additionally, the claims indicates that the media composition can be in a frozen state preparations. The invention disclosed by Ponting is to provide a completely defined media (column 1). Ponting teaches that the disclosed media can be used for variety of cell types and that the defined media 'makes possible the precise determination of the effect of a known molecule" Column 7, lines 44-50). Further, Ponting teaches that in determining the effective amount of any of the constituent components experimentation by methods known to a cell culturist would have to be done (bridging columns 8-9 and generally supported by the working examples). Finally, Ponting teaches that specific conditions for culturing a particular cell type would have to be adapted by substituting the serum-supplement to the methods and materials known in the art that would have been used for any particular cell type (starting in column 15, section E). Though Ponting does not specifically teach to use such factors as LIF, iron-saturated transferrin or lipid poor and recombinant albumin, these factors were readily available at the time of filing and used in cell culturing. For example, at the time of filing it was well known that mouse embryonic stem cells required LIF in the culture media to efficiently maintain their undifferentiated state during culturing, therefore, ti would be obvious to include this factor in the propagation of embryonic stem cells. Further, if the mouse ES cells were to be used in methods of differentiation or if the culture was human embryonic stem cells which were known not to be responsive to the presence or absence of LIF, this factor would be excluded from the media. As noted above, the teaching of Ponting anticipates the specific embodiments encompassed by claims 89-103, 105-111, 117-

127, 129, 131, 133, 135, 137,139, 141, 143, 145, 147, 151, 153, 157-159, 161-164, 166, 167, 169-172, and though Ponting does not specifically disclose the specific components listed in the remaining claims, the use of these components would be obvious because they are factors commonly used in cell culture. Further, Ponting teaches that the media should be as defined as possible and optimized for a given cell type, therefore one would be motivated to use and test the various forms of these components for their specific affects on the cells in culture. For example lipid-poor albumin provides a more defined source of albumin, lacking lipids that could affect the cells. Moreover, Ponting teaches that the components can be natural or synthetic (column 11, lines 65-68), wherein a synthetic component would represent a more defined molecule free from potential contaminants that may be present in naturally isolated sources. The level of knowledge and skill in the art for culturing cells is high, and there would be a reasonable motivation and expectation of success to use specific components from various sources as generally taught by Ponting to provide for a more defined and optimized media. Upon review of the present specification, there is no specific teaching that any one of the components recited or encompassed by the instant claims provides any unexpected affect on the cultured cells that would not have been readily known in the art, such as the use of LIF or feeder cells to maintain embryonic stem cells in culture.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

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